[redacted]ENT COOPERATION TREA[redacted]

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
2779/2/PCT		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/ US 94/ 12720	14/11/94	30/11/93
Applicant		
G.D. SEARLE & CO. et al.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 7 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. [X] **Certain claims were found unsearchable** (see Box I).

2. [ ] **Unity of invention is lacking** (see Box II).

3. [ ] The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing
   - [ ] filed with the international application.
   - [ ] furnished by the applicant separately from the international application,
     - [ ] but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
   - [ ] Transcribed by this Authority

4. With regard to the **title,**
   - [X] the text is approved as submitted by the applicant.
   - [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   - [X] the text is approved as submitted by the applicant.
   - [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:

   Figure No. _____
   - [ ] as suggested by the applicant.
   - [ ] because the applicant failed to suggest a figure.
   - [ ] because this figure better characterizes the invention.
   - [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

tional application No.
PCT/US94/12720

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

REMARK : ALTHOUGH CLAIMS 37 - 59 ARE DIRECTED TO A METHOD OF TREATMENT OF (DIAGNOSTIC METHOD PRACTISED ON) THE HUMAN/ANIMAL BODY THE SEARCH HAS BEEN CARRIED OUT AND BASED ON THE ALLEGED EFFECTS OF THE COMPOUND/COMPOSITION.

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

1,2,14,19,20,32,37,38,50 and 55-59

SEE ATTACHED SHEET

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/

As the drafting of claim 1 encompasses such an enormous amount of compounds (cf. definitions of R^1 - R^4 in connection with the last proviso: "R^4 is aryl substituted with sulfamyl or R^6 is sulfamyl when R^1 is phenyl not substituted with sulfamyl" [i.e., if R^1 is aryl (or heteroaryl) other than phenyl, the sulfamyl group does not have to be present]), a complete search is not possible on economic grounds (see WIPO: PCT Search Guidelines; Chapter III, 2).

Therefore, the search has been limited to the compounds of claim 1, wherein R^1 = (subst.) phenyl.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 94/12720

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D231/12 A61K31/415 C07D231/14 C07D231/16 C07D231/18
C07D231/54 C07D401/04 C07D403/04 C07D405/04 C07D409/04
C07D495/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 116, no. 1, 6 January 1992, Columbus, Ohio, US; abstract no. 6480s, H.M. MOKHTAR ET AL. 'Synthesis of nitrogenous compounds. part III.' page 643 ;column 2 ; see abstracts and Chemical Abstract, CHEMICAL SUBSTANCE INDEX, vol. 116, 1992, page 1497CS: RN [137272-44-7] & PAK. J. SCI. IND. RES., vol.34, no.1, 1991 pages 9 - 15 cited in the application --- -/--	1-5

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 March 1995	23.03.95

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+ 31-70) 340-3016	Fink, D

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 114, no. 21, 27 May 1991, Columbus, Ohio, US; abstract no. 207194j, H.M. MOKHTAR ET AL 'Synthesis of nitrogenous compounds. Part II.' page 824 ;column 2 ; see abstract snd Chemical Abstracts, CHEMICAL SUBSTANCES, 12th Collective Index, vol. 106-115, 1987-1991, page 78406CS: RN [133506-86-2], [133507-34-3] and [133507-39-8] & PAK. J. SCI. IND. RES., vol.33, no.1-2, 1990 pages 30 - 36 ---	1-6
X	CHEMICAL ABSTRACTS, vol. 111, no. 25, 18 December 1989, Columbus, Ohio, US; abstract no. 232651b, H.M. MOKHTAR ET AL. 'Synthesis of nitrogenous compounds from d-unsaturated 1,3-dicarbonyl esters. Part I.' page 775 ;column 1 ; see abstract and Chemical Abstracts, CHEMICAL SUBSTANCES, 12th Collective Index, vol. 106-115, 1987-1991, page12839CS: RN [123910-00-9] and page 78406CS: RN [123909-33-1], [123090-21-7], [123909-29-5] and [123909-15-9] & J. CHEM. SOC. PAK., vol.10, no.4, 1988 pages 414 - 424 ---	1-6
X	CHEMICAL ABSTRACTS, vol. 111, no. 7, 14 August 1989, Columbus, Ohio, US; abstract no. 57614t, HM. MOKHTAR 'Synthesis of trisubstituted pyrazoles with possible antimicrobial activity.' page 749 ;column 1 ; see abstract and Chemical Abstracts, CHEMICAL SUBSTANCES, 12th Collective Index, vol. 106-115, 1987-1991, page 12844CS: RN [121650-33-7] & PAK. J. SCI. IND. RES., vol.31, no.11, 1988 pages 762 - 767 cited in the application --- -/--	1-5

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 100, no. 5, 30 January 1984, Columbus, Ohio, US; abstract no. 34458d, R. SOLIMAN ET AL. 'Synthesis and antidiabetic activity of some sulfonylurea derivatives of 3,5-disubstituted pyrazoles' page 444 ;column 2 ; see abstract and Chemical Abstracts, CHEMICAL SUBSTANCES, 11th Collective Index, vol. 96-105, 1982-1986, page 58036CS: RN [88289-69-4], [88289-68-3], [88289-72-9] and [88289-71-8] & J. PHARM. SCI., vol.72, no.9, 1983 pages 999 - 1004 ---	1-6
X	CHEMICAL ABSTRACTS, vol. 95, no. 11, 14 September 1981, Columbus, Ohio, US; abstract no. 97662q, R. SOLIMAN ET AL. 'Preparation and antidiabetic activity of new substituted 3-methyl-5-phenylpyrazolesulfonylurea derivatives.' page 642 ;column 2 ; see abstract and Chemical Abstracts, CHEMICAL SUBSTANCES, 10th Collective Index, vol. 86-95, 1977-1981, page 7480CS: RN [78794-41-9] & J. PHARM. SCI., vol.70, no.6, 1981 pages 602 - 605 cited in the application ---	1-6
X	EP,A,0 418 845 (FUJISAWA PHARMACEUTICAL CO., LTD.) 27 March 1991 cited in the application see page 55; claim 1 see page 32-41; examples 14.2, 15.3, 15.4, 17.3, 19.1, 19.2, 22.1 and 22.2 see page 21, line 54 - page 22, line 12 ---	1,2,19, 20,37, 38,55-59
X	EP,A,0 554 829 (FUJISAWA PHARMACEUTICAL CO., LTD.) 11 August 1993 see page 30; claim 1 see pages 20-27; examples 6.1, 6.5, 6.7, 8.1, 8.7, 8.10, 9, 13.5 and 26.2 see page 16, line 36 - line 52 ---	1,2,19, 20,37, 38,55-59
	-/--	

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US,A,4 146 721 (G. RAINER) 27 March 1979 see column 1, line 16 - line 51 see column 16; example 19 see column 25; example 47 see column 34, line 39 - line 47 ---	1,2,19, 20,37, 38,55-59
X	CHEMICAL ABSTRACTS, vol. 121, no. 11, 12 September 1994, Columbus, Ohio, US; abstract no. 134017m, M.S.I MAKKI ET AL. 'Pyrazole derivatives. Part I. Synthesis and spectra of trisubstituted pyrazoline and pyrazole derivatives with possible hypoglycemic activity.' page 1023 ;column 1 ; see abstract and RN [156849-15-9] and [156849-12-6] & INT. J. CHEM., vol.4, no.4, 1993 pages 117 - 128 -----	1,2

2

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 94/12720

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP-A-0418845	27-03-91	AU-B-	637142	20-05-93
		AU-A-	6307290	18-04-91
		CN-A-	1050382	03-04-91
		JP-A-	3141261	17-06-91
		US-A-	5134142	28-07-92
EP-A-0554829	11-08-93	AU-A-	3217493	12-08-93
		CA-A-	2088835	06-08-93
		CN-A-	1075959	08-09-93
		JP-A-	5246997	24-09-93
US-A-4146721	27-03-79	DE-A-	1946370	22-04-71
		US-A-	4325962	20-04-82
		AT-A,B	313274	15-01-74
		AT-A,B	304534	15-12-72
		BE-A-	755924	15-02-71
		CA-A-	959838	24-12-74
		CH-A-	583707	14-01-77
		CH-A-	587251	29-04-77
		DE-A-	2141124	24-02-72
		FR-A,B	2070689	17-09-71
		GB-A-	1307005	14-02-73
		NL-A-	7013384	16-03-71
		SE-B-	385212	14-06-76

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
Searle 27 891		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 94/ 12720	14/11/1994	30/11/1993
International Patent Classification (IPC) or national classification and IPC		
C07D231/12		
Applicant		
G.D. SEARLE & CO. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This **REPORT** consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by **ANNEXES**, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consists of a total of 21 sheets.

3. This report contains indications and corresponding pages relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23/05/1995	12.12.95
Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	J. Barthl Wagner
	Telephone No.

Intern. application No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT PCT/US94/12720

I. Basis of the report

1. This report has been drawn up on the basis of (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

[ ] the international application as originally filed.

[x] the description, pages 1-183, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____,

[x] the claims, Nos. _____, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. 1-20, filed with the letter of 03.11.95,
Nos. _____, filed with the letter of _____,

[ ] the drawings, sheets/fig _____, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:
[ ] the description, pages _____.
[ ] the claims, Nos. _____.
[ ] the drawings, sheets/fig _____.

3. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-3,12,14	YES
	Claims 4-11,13,15-20	NO
Inventive Step (IS)	Claims	YES
	Claims 1-20	NO
Industrial Applicability (IA)	Claims 1-20	YES
	Claims	NO

2. CITATIONS AND EXPLANATIONS

1). Although claim 1 and also the other independent claims comprise various provisos claims 1-3, 12 and 14 encompass compounds or compositions already known from the prior art documents cited in the international search report. Compounds which have a sulfamyl-phenyl substituent in 1- or 5-position of the pyrazole and which are encompassed by the claims are disclosed in
Chem. Abstr., Vol.111, N°232651b
Chem. Abstr., Vol.114, N°207195k or
Chem. Abstr., Vol.100, N° 34457c.

2). Particularly relevant for the evaluation of inventive step of the claimed subject-matter are
D1: EP-A-0 418 845
D2: EP-A-0 554 829
D3: US-A-4 146 721;
D1 to D3 disclose pyrazole compounds with antiinflammatoty activity. In the light of the prior art the problem to be solved by the present invention is

seen in the provision of further antiinflammatory agents. The claimed solution cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons. The antiinflammatory compounds disclosed in D1 to D3 are structurally closely related to the claimed compounds; i.e. the claimed compounds are distinguished by the various provisos only. The claimed compounds comprise all the essential structural elements of the known NSAIDs so that a skilled person would have expected that they will have similar therapeutic activities. An inventive step could thus only be acknowledged for novel compounds if it could be shown that they differ from the known compounds by a common novel feature which contributes to any unexpected advantage or property of the claimed compounds. From the description it can be taken that the claimed compounds selectively inhibit cyclooxygenase II over cyclooxygenase I. However such a selectivity ratio could only indicate an inventive step if it is shown to be unexpectedly improved in comparison with the structurally closest prior art compounds.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The application contains various independent claims of the same category and does thus not meet the requirements of Article 6 PCT because the claims as a whole are not clear and concise. In claim 12 the first proviso is not clear because formula II does not contain a substituent R^1.

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

To:

United States Patent and Trademark Office
(Box PCT)
Washington D.C. 20231
United States of America

in its capacity as elected Office

NOTIFICATION CONCERNING DOCUMENT TRANSMITTED

Date of mailing (day/month/year)
18 December 1995 (18.12.95)

International application No.
PCT/US94/12720

International filing date (day/month/year)
14 November 1994 (14.11.94)

Applicant
G. D. SEARLE & CO. et al

The International Bureau transmits herewith the following documents and number thereof:

_____ copy of the international preliminary examination report and annexes (Article 36(3)(a))

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer
S. Mafla

Telephone No.: (41-22) 730.91.11

[redacted]TENT COOPERATION TRE[redacted]

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
Searle 27 891		
International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/US 94/ 12720	14/11/1994	30/11/1993
International Patent Classification (IPC) or national classification and IPC		
C07D231/12		
Applicant		
G.D. SEARLE & CO. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consists of a total of 21 sheets.

3. This report contains indications and corresponding pages relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23/05/1995	30.01.96
Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	J. Barthl-Wagner Telephone No.

I. Basis of the report

1. This report has been drawn up on the basis of (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

[ ] the international application as originally filed.

[x] the description, pages 1-183, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____,

[x] the claims, Nos. _____, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. 2part,3part,7part,8-11,12part,13part,14-20, filed with the letter of 03.11.95,
Nos. 1,2part,3part,4-6,7part,12part,13part___, filed with the letter of 16.01.96,

[ ] the drawings, sheets/fig _____, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:
[ ] the description, pages _____.
[ ] the claims, Nos. _____.
[ ] the drawings, sheets/fig _____.

3. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-20	YES
	Claims	NO
Inventive Step (IS)	Claims	YES
	Claims 1-20	NO
Industrial Applicability (IA)	Claims 1-20	YES
	Claims	NO

2. CITATIONS AND EXPLANATIONS

1). After the insertion of further provisos into the claims the claimed subject-matter appears to be limited also vis-à-vis
Chem. Abstr., Vol.111, N˚232651b
Chem. Abstr., Vol.114, N˚207194j and
Chem. Abstr., Vol.100, N˚ 34458d.
The present application seems thus to satisfy the criterion set forth in Art. 33(2) PCT.

2). Particularly relevant for the evaluation of inventive step of the claimed subject-matter are
D1: EP-A-0 418 845
D2: EP-A-0 554 829
D3: US-A-4 146 721;
D1 to D3 disclose pyrazole compounds with antiinflammatoty activity. In the light of the prior art the problem to be solved by the present invention is

seen in the provision of further antiinflammatory agents. The claimed solution cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons. The antiinflammatory compounds disclosed in D1 to D3 are structurally closely related to the claimed compounds; i.e. the claimed compounds are distinguished by the various provisos only. The claimed compounds comprise all the essential structural elements of the known NSAIDs so that a skilled person would have expected that they will have similar therapeutic activities. An inventive step could thus only be acknowledged for novel compounds if it could be shown that they differ from the known compounds by a common novel feature which contributes to any unexpected advantage or property of the claimed compounds. From the description it can be taken that the claimed compounds selectively inhibit cyclooxygenase II over cyclooxygenase I. However such a selectivity ratio could only indicate an inventive step if it is shown to be unexpectedly improved in comparison with the structurally closest prior art compounds.

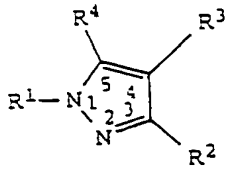
VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The application contains various independent claims of the same category and does thus not meet the requirements of Article 6 PCT because the claims as a whole are not clear and concise. In claim 12 the first proviso is not clear because formula II does not contain a substituent R^1.

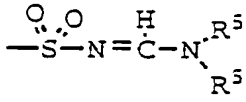
What is claimed is:

1. A compound of Formula I



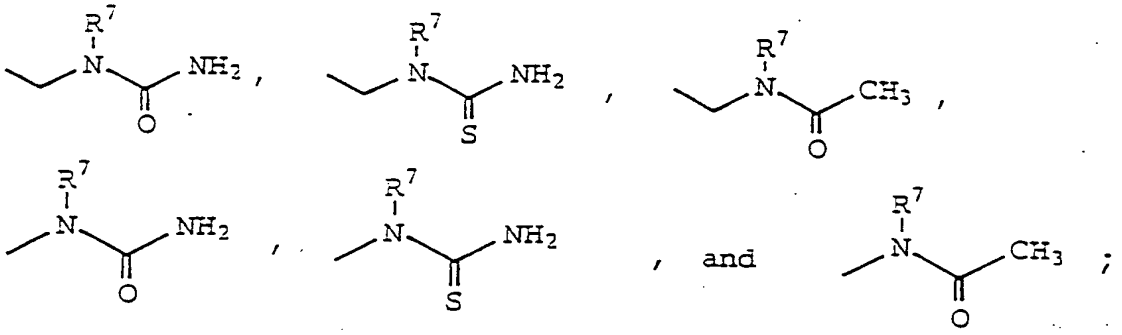
(I)

wherein R^1 is phenyl substituted at a substitutable position with one or more radicals selected from halo, C_1-C_{10}-alkyl, sulfamyl and



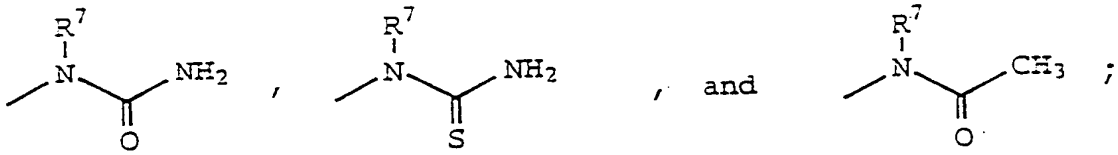
;

wherein R^2 is selected from hydrido, C_1-C_{10}-alkyl, C_1-C_6-haloalkyl, cyano, carboxyl, C_1-C_6-alkoxycarbonyl, C_1-C_6-carboxyalkyl, C_1-C_{10}-cyanoalkyl, C_1-C_6-alkoxycarbonylcyano-C_2-C_6-alkenyl, C_1-C_6-haloaralkyl, C_1-C_6-carboxyhaloalkyl, C_1-C_6-alkoxycarbonyl-C_1-C_{10}-haloalkyl, C_1-C_6-aminocarbonyl-C_1-C_{10}-haloalkyl, C_1-C_{10}-alkylaminocarbonyl-C_1-C_{10}-haloalkyl, C_1-C_6-N-alkylamino, C_1-C_6-N,N-dialkylamino, N-arylamino, C_1-C_6-N-aralkylamino, C_1-C_6-N-alkyl-N-aryl-C_1-C_6-alkylamino, C_1-C_6-N-alkyl-N-arylamino, C_1-C_6-aminoalkyl, C_1-C_6-N-alkylamino-C_1-C_6-alkyl, C_1-C_6-N,N-dialkylaminoalkyl, C_1-C_6-N-arylaminoalkyl, C_1-C_6-N-aryl-C_1-C_6-alkylaminoalkyl, C_1-C_6-N-alkyl-N-aryl-C_1-C_6-alkylaminoalkyl, C_1-C_6-N-alkyl-N-arylamino-C_1-C_6-alkyl, C_1-C_6-alkoxy, aryloxy, C_1-C_6-aralkoxy, C_1-C_6-alkylthio, arylthio, C_1-C_6-aralkylthio, aminocarbonyl, C_1-C_6-aminocarbonylalkyl, C_1-C_6-N-alkylaminocarbonyl, N-arylaminocarbonyl, C_1-C_6-N,N-dialkylaminocarbonyl, C_1-C_6-N-alkyl-N-arylaminocarbonyl, C_3-C_7-cycloalkylaminocarbonyl, C_1-C_6-carboxyalkylaminocarbonyl, C_1-C_6-aralkoxycarbonyl-C_1-C_6-alkylaminocarbonyl, C_1-C_6-hydroxyalkyl,



wherein R^3 is selected from hydrido, C_1-C_{10}-alkyl, halo, cyano, C_1-C_6-hydroxyalkyl, C_1-C_6-alkoxy, C_1-C_6-alkylthio, C_1-C_6-N-alkylamino, C_1-C_6-N,N-dialkylamino, C_1-C_6-alkylsulfonyl and C_3-C_7-cycloalkyl;

wherein R^4 is selected from aryl-C_2-C_6— alkenyl, aryl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkenyl and five to ten membered heterocyclic; wherein R^4 is optionally substituted at a substitutable position with one or more radicals selected from halo, C_1-C_6-alkylthio, C_1-C_6-alkylsulfinyl, C_1-C_{10}-alkyl, C_2-C_6-alkenyl, C_1-C_6-alkylsulfonyl, cyano, carboxyl, C_1-C_6-alkoxycarbonyl, aminocarbonyl, C_1-C_6-haloalkyl, hydroxyl, C_1-C_6-alkoxy, C_1-C_6-hydroxyalkyl, C_1-C_6-haloalkoxy, sulfamyl, C_1-C_6-alkylaminocarbonyl, amino, C_1-C_6-N-alkylamino, C_1-C_6-N,N-dialkylamino, five or six membered heterocyclic, C_3-C_7-cycloalkyl-C_1-C_{10}-alkyl, nitro,



wherein R^5 is C_1-C_{10}-alkyl; and

wherein R^7 is selected from hydrido, C_1-C_{10}-alkyl, aryl, and aryl-C_1-C_{10}-alkyl,

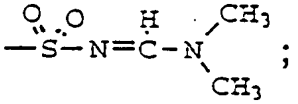
wherein aryl wherever occuring means phenyl, naphthyl, tetrahydronaphthyl, indane, biphenyl,

provided R^2 and R^3 are not identical radicals selected from hydrido, carboxyl and ethoxycarbonyl; further provided that R^2 is not carboxyl or methyl when R^3 is hydrido and when R^4 is phenyl; further provided that R^4 is not triazolyl when

R^2 is methyl; further provided that R^4 is not aralkenyl when R^2 is carboxyl, aminocarbonyl or ethoxycarbonyl; further provided that R^4 is not phenyl when R^2 is methyl and R^3 is carboxyl; further provided that R^4 is not 4-chlorophenyl when R^2 is methyl and R^3 is bromo; further provided that R^4 is not unsubstituted thienyl when R^2 is trifluoromethyl; and further provided that R^4 is aryl substituted with sulfamyl, when R^1 is phenyl not substituted with sulfamyl,

or a pharmaceutically-acceptable salt thereof.

2. Compound of Claim 1 wherein R^1 is phenyl, substituted at a substitutable position with one or more radicals selected from fluoro, chloro, methyl, sulfamyl and



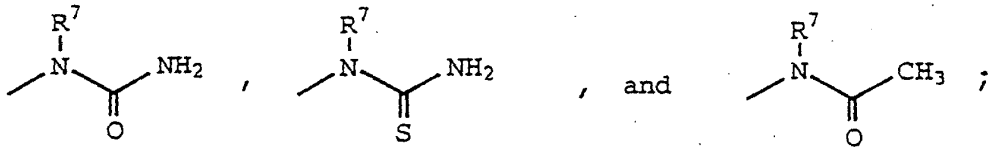
wherein R^2 is selected from hydrido, methyl, ethyl, isopropyl, *tert*-butyl, isobutyl, hexyl, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, cyano, carboxyl, methoxycarbonyl, ethoxycarbonyl, isopropoxycarbonyl, *tert*-butoxycarbonyl, propoxycarbonyl, butoxycarbonyl, isobutoxycarbonyl, pentoxycarbonyl, acetyl, propionyl, butyryl, isobutyryl, valeryl, isovaleryl, pivaloyl, hexanoyl, trifluoroacetyl, cyanomehtyl, ethoxycarbonylcyanoethenyl, 1,1-difluoro-1-phenylmethyl, 1,1-difluoro-1-phenylethyl, difluoroacetyl, methoxycarbonyldifluoromethyl, difluoroacetamidyl, N,N-dimethyldifluoroacetamidyl, N-phenyldifluoroacetamidyl, N-ethylamino, N-methylamino, N,N-dimethylamino, N,N-diethylamino, N-phenylamino, N-benzylamino, N-phenylethylamino, N-methyl-N-benzylamino, N-ethyl-N-phenylamino, N-methyl-N-phenylamino, aminomethyl, N-methylaminomethyl, N,N-

dimethylaminomethyl, N-phenylaminomethyl, N-benzylaminomethyl, N-methyl-N-benzylaminomethyl, N-methyl-N-phenylaminomethyl, methoxy, ethoxy, phenoxy, benzyloxy, methylthio, phenylthio, benzylthio, N-methylurea, N-methylthiourea, N-methylacetamidyl, urea, ureamethyl, thiourea, thioureamethyl, acetamidyl, N-phenylthioureamethyl, N-benzylthioureamethyl, N-methylthioureamethyl, N-phenylureamethyl, N-benzylureamethyl, N-methylureamethyl, N-phenylacetamidylmethyl, N-benzylacetamidylmethyl, N-methylacetamidylmethyl, aminocarbonyl, aminocarbonylmethyl, N-methylaminocarbonyl, N-ethylaminocarbonyl, N-isopropylaminocarbonyl, N-propylaminocarbonyl, N-butylaminocarbonyl, N-isobutylaminocarbonyl, N-*tert*-butylaminocarbonyl, N-pentylaminocarbonyl, N-phenylaminocarbonyl, N,N-dimethylaminocarbonyl, N-methyl-N-ethylaminocarbonyl, N-(3-fluorophenyl)aminocarbonyl, N-(4-methylphenyl)aminocarbonyl, N-(3-chlorophenyl)aminocarbonyl, N-methyl-N-(3-chlorophenyl)aminocarbonyl, N-(4-methoxyphenyl)aminocarbonyl, N-methyl-N-phenylaminocarbonyl, cyclopentylaminocarbonyl, cyclohexylaminocarbonyl, carboxymethylaminocarbonyl, benzyloxycarbonylmethylaminocarbonyl, hydroxypropyl, hydroxymethyl, and hydroxypropyl;

wherein R^3 is selected from hydrido, methyl, ethyl, isopropyl, *tert*-butyl, isobutyl, hexyl, fluoro, chloro, bromo, cyano, methoxy, methylthio, methylsulfonyl, N-methylamino, N-ethylamino, N,N-dimethylamino, N,N-diethylamino, cyclopropyl, cyclopentyl, hydroxypropyl, hydroxymethyl, and hydroxyethyl; and

wherein R^4 is selected from phenylethenyl, phenyl, naphthyl, biphenyl, cyclohexyl, cyclopentyl,

cycloheptyl, 1-cyclohexenyl, 2-cyclohexenyl, 3-cyclohexenyl, 4-cyclohexenyl, 1-cyclopentenyl, 4-cyclopentenyl, benzofuryl, 2,3-dihydrobenzofuryl, 1,2,3,4-tetrahydronaphthyl, benzothienyl, indenyl, indanyl, indolyl, dihydroindolyl, chromanyl, benzopyran, thiochromanyl, benzothiopyran, benzodioxolyl, benzodioxanyl, pyridyl, thienyl, thiazolyl, oxazolyl, furyl and pyrazinyl; wherein R^4 is optionally substituted at a substitutable position with one or more radicals selected from fluoro, chloro, bromo, methylthio, methylsulfinyl, methyl, ethyl, propyl, isopropyl, *tert*-butyl, isobutyl, hexyl, ethylenyl, propenyl, methylsulfonyl, cyano, carboxyl, methoxycarbonyl, ethoxycarbonyl, isopropoxycarbonyl, *tert*-butoxycarbonyl, propoxycarbonyl, butoxycarbonyl, isobutoxycarbonyl, pentoxycarbonyl, aminocarbonyl, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, bromodifluoromethyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, hydroxyl, methoxy, methylenedioxy, ethoxy, propoxy, n-butoxy, sulfamyl, methylaminosulfonyl, hydroxypropyl, hydroxyisopropyl, hydroxymethyl, hydroxyethyl, trifluoromethoxy, amino, N-methylamino, N-ethylamino, N-ethyl-N-methylamino, N,N-dimethylamino, N,N-diethylamino, formylamino, methylcarbonylamino, trifluoroacetamino, piperadinyl, piperazinyl, morpholino, cyclohexylmethyl, cyclopropylmethyl, cyclopentylmethyl, nitro,



and

wherein R^7 is selected from hydrido, methyl, ethyl, phenyl and benzyl;

or a pharmaceutically-acceptable salt thereof.

3. Compound of Claim 2 selected from compounds, and their pharmaceutically acceptable salts, of the group consisting of

ethyl 1-[4-(aminosulfonyl)phenyl]-5-(4-chlorophenyl)-1H-pyrazole-3-carboxylate;

ethyl 1-[4-(aminosulfonyl)phenyl]-5-(4-methylphenyl)-1H-pyrazole-3-carboxylate;

isopropyl 1-[4-(aminosulfonyl)phenyl]-5-(4-chlorophenyl)-1H-pyrazole-3-carboxylate;

N-[4-methylphenyl]-1-[4-(aminosulfonyl)phenyl]-5-(4-fluorophenyl)-1H-pyrazole-3-carboxamide;

N-[3-chlorophenyl]-1-[4-(aminosulfonyl)phenyl]-5-(4-fluorophenyl)-1H-pyrazole-3-carboxamide;

N-[3-fluorophenyl]-1-[4-(aminosulfonyl)phenyl]-5-(4-fluorophenyl)-1H-pyrazole-3-carboxamide;

N-[3-fluorophenyl]-1-[4-(aminosulfonyl)phenyl]-5-(4-chlorophenyl)-1H-pyrazole-3-carboxamide;

phenylmethyl N-[[1-[4-(aminosulfonyl)phenyl]-5-(4-chlorophenyl)-1H-pyrazol-3-yl]carbonyl]glycinate;

4-[5-(4-bromophenyl)-3-cyano-1H-pyrazol-1-yl]benzenesulfonamide;

4-[3-cyano-5-(4-fluorophenyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-chlorophenyl)-3-cyano-1H-pyrazol-1-yl]benzenesulfonamide;

4-[3-cyano-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[3-cyano-5-(4-methylphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[3-cyano-5-(4-methylthiophenyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(5-chloro-4-methoxyphenyl)-3-cyano-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(5-bromo-4-methoxyphenyl)-3-cyano-1H-pyrazol-1-yl]benzenesulfonamide;

4-[3-cyano-5-phenyl-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-chloro-5-(4-fluorophenyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[4-chloro-5-(4-chlorophenyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[4-bromo-5-(4-chlorophenyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[4-chloro-5-phenyl-1H-pyrazol-1-yl]benzenesulfonamide;
4-[4-chloro-5-(3,5-dichloro-4-methoxyphenyl)-1H-pyrazol- 1-yl]benzenesulfonamide;
4-[4-bromo-5-(4-methylphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[4-chloro-5-(4-methylphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[4-chloro-5-(3-chloro-4-methoxyphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[4-chloro-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[4-bromo-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[4-cyano-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[4-ethyl-5-phenyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[4-methyl-5-phenyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[5-(4-methoxyphenyl)-4-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[5-(4-chlorophenyl)-4-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[5-(4-chlorophenyl)-4-ethyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[4-ethyl-5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-ethyl-5-(4-methoxy-3-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-ethyl-5-(4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-ethyl-5-(3-fluoro-4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-fluorophenyl)-4-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-methyl-5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-fluoro-5-phenyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-bromo-5-(4-chlorophenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-chloro-5-(3,5-dichloro-4-methoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-chloro-3-(difluoromethyl)-5-phenyl-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-bromo-3-(difluoromethyl)-5-phenyl-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-chloro-3-(difluoromethyl)-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-chloro-3-cyano-5-phenyl-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-chloro-5-(4-chlorophenyl)-3-cyano-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-chloro-3-cyano-5-(4-fluorophenyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-bromo-3-cyano-5-(4-fluorophenyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-bromo-3-cyano-5-phenyl-1H-pyrazol-1-yl]benzenesulfonamide;

ethyl [1-(4-aminosulfonylphenyl)-4-bromo-5-(4-chlorophenyl)-1H-pyrazol-3-yl]carboxylate;

methyl [1-(4-aminosulfonylphenyl)-4-chloro-5-phenyl-1H-pyrazol-3-yl]carboxylate;
methyl [1-(4-aminosulfonylphenyl)-4-chloro-5-(4-chlorophenyl)-1H-pyrazol-3-yl]carboxylate;
ethyl [1-(4-aminosulfonylphenyl)-4-chloro-5-(4-chlorophenyl)-1H-pyrazol-3-yl]carboxylate;
methyl [1-(4-aminosulfonylphenyl)-4-chloro-5-(4-fluorophenyl)-1H-pyrazol-3-yl]carboxylate;
methyl [1-(4-aminosulfonylphenyl)-4-bromo-5-(4-fluorophenyl)-1H-pyrazol-3-yl]carboxylate;
methyl [1-(4-aminosulfonylphenyl)-4-chloro-5-(3-chloro-4-methoxyphenyl)-1H-pyrazol-3-yl]carboxylate;
methyl [1-(4-aminosulfonylphenyl)-4-chloro-5-(3,5-dichloro-4-methoxyphenyl)-1H-pyrazol-3-yl]carboxylate;
methyl [1-(4-aminosulfonylphenyl)-5-(3-bromo-4-methoxyphenyl)-4-chloro-1H-pyrazol-3-yl]carboxylate;
4-[4-chloro-3-isopropyl-5-phenyl-1H-pyrazol-1-yl]benzenesulfonamide;
4-[4-chloro-3-methyl-5-phenyl-1H-pyrazol-1-yl]benzenesulfonamide;
4-[4-chloro-3-hydroxymethyl-5-phenyl-1H-pyrazol-1-yl]benzenesulfonamide;
4-[4-chloro-5-(4-chlorophenyl)-3-hydroxymethyl-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[5-phenyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[5-(4-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[5-(4-cyanophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[5-(2,4-difluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-bromophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(2,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(2-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(2-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-aminophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(2-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-fluoro-2-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-ethoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3,5-dimethylphenyl-4-methoxy)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-fluoro-4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-methylthiophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-chloro-3-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-ethylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(2,4-dimethylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(2-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-methoxy-3-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-bromo-4-methylthiophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-chloro-4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3,4-dimethoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-chloro-4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-chloro-4-methoxy-5-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-ethyl-4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-fluoro-2-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-methoxy-3-(3-propenyl)phenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3,5-dichloro-4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-chloro-4-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-fluoro-4-methylthiophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-methyl-4-methylthiophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

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4-[5-(3-chloro-4-methylthiophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-(N,N-dimethylamino)phenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-methyl-3-nitrophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-(N-methylamino)phenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-amino-4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-chlorophenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-methylthiophenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-methylphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-phenyl-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-methoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-fluoro-4-methoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-chlorophenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(2-fluoro-4-methoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-chloro-4-methylphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-chloro-4-methoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-chloro-3-methylphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3,4-dimethoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3,5-dichloro-4-methoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3,5-difluoro-4-methoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(2-methoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-bromo-4-methoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-methylsulfonylphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-chlorophenyl)-3-(heptafluoropropyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-chlorophenyl)-3-(chloro-difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-chlorophenyl)-3-(pentafluoroethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-fluorophenyl)-3-(3-hydroxypropyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3,5-dichloro-4-methoxyphenyl)-3-(3-hydroxypropyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-chloro-4-methoxyphenyl)-3-(chloromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-chlorophenyl)-3-(cyanomethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[3-(chloro-difluoromethyl)-5-(3-fluoro-4-methoxyphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;

ethyl 3-[1-(4-aminosulfonylphenyl)-5-(phenyl)-1H-pyrazol-3-yl]-2-cyano-2-propenoate;

4-[5-(phenyl)-3-(fluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(5-bromo-2-thienyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(5-chloro-2-thienyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(1-cyclohexenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(cyclohexyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(1,4-benzodioxan-6-yl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[3-(difluoromethyl)-5-(4-methylcyclohexyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(2-benzofuranyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(1,3-benzodioxol-5-yl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(2-benzofuryl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(5-bromo-2-thienyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(5-chloro-2-thienyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(5-indanyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(5-methyl-2-thienyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(2,3-dihydrobenzofuran-2-yl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(1-cyclohexenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(1,2,3,4-tetrahydronaphth-5-yl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(2-benzothienyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3,4-dihydro-2H-1-benzothiopyran-7-yl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

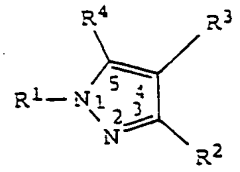
4-[5-(4-methyl-1,3-benzodioxol-6-yl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide; and
4-[5-(4-methyl-1,3-benzodioxol-5-yl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide.

4. Compound of Claim 2 where the compound is 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide, or a pharmaceutically-acceptable salt thereof.

5. Compound of Claim 2 where the compound is 4-[5-(4-chlorophenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide, or a pharmaceutically-acceptable salt thereof.

6. Compound of Claim 2 where the compound is 4-[5-(3-fluoro-4-methoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide, or a pharmaceutically-acceptable salt thereof.

7. A compound of Formula I

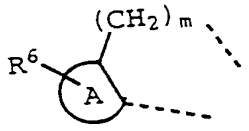


(I)

wherein R^1 is phenyl substituted at a substitutable position with sulfamyl;

wherein R^2 is selected from C_1-C_6-haloalkyl, cyano, carboxyl, C_1-C_6-alkoxycarbonyl, C_1-C_6-carboxyalkyl, aminocarbonyl, C_1-C_6-N-alkylaminocarbonyl, N-arylaminocarbonyl, C_1-C_6-N,N-dialkylaminocarbonyl, C_1-C_6-N-alkyl-N-arylaminocarbonyl, C_3-C_7-cycloalkylaminocarbonyl and C_1-C_6-hydroxyalkyl;

wherein R^3 and R^4 together form



;

wherein m is 2;

wherein A is selected from phenyl and five membered heteroaryl; and

wherein R^6 is one or more radicals selected from halo, C_1-C_{10}-alkyl, C_1-C_6-alkylsulfonyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, amino and nitro;

wherein aryl wherever occuring means phenyl, naphthyl, tetrahydronaphthyl, indane, biphenyl;

or a pharmaceutically-acceptable salt thereof.

8. Compound of Claim 7 wherein R^2 is

selected from fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, cyano, carboxyl, methoxycarbonyl, ethoxycarbonyl, isopropoxycarbonyl, tert-butoxycarbonyl, propoxycarbonyl, butoxycarbonyl, isobutoxycarbonyl, pentoxycarbonyl, acetyl, propionyl, butyryl, isobutyryl, valeryl, isovaleryl, pivaloyl, hexanoyl, trifluoroacetyl, aminocarbonyl, N-methylaminocarbonyl, N-ethylaminocarbonyl, N-isopropylaminocarbonyl, N-propylaminocarbonyl, N-butylaminocarbonyl, N-isobutylaminocarbonyl, N-tert-butylaminocarbonyl, N-pentylaminocarbonyl, N-phenylaminocarbonyl, N,N-dimethylaminocarbonyl, N-

methyl-N-ethylaminocarbonyl, N-(3-fluorophenyl)aminocarbonyl, N-(4-methylphenyl)aminocarbonyl, N-(3-chlorophenyl)aminocarbonyl, N-(4-methoxyphenyl)aminocarbonyl, N-methyl-N-phenylaminocarbonyl, cyclohexylaminocarbonyl, hydroxypropyl, hydroxymethyl and hydroxyethyl; wherein A is selected from phenyl, furyl and thienyl; and wherein R^6 is one or more radicals selected from fluoro, chloro, bromo, methylsulfonyl, methyl, ethyl, isopropyl, *tert*-butyl, isobutyl, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl,

dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, methoxy, methylenedioxy, ethoxy, propoxy, n-butoxy, amino, and nitro;

or a pharmaceutically-acceptable salt thereof.

9. Compound of Claim 8 selected from compounds, and their pharmaceutically acceptable salts, of the group consisting of

4-[3-(difluoromethyl)-4,5-dihydro-7-methoxy-1H-benz[g]indazol-1-yl]benzenesulfonamide;

4-[3-(difluoromethyl)-4,5-dihydro-7-methyl-1H-benz[g]indazol-1-yl]benzenesulfonamide;

4-[4,5-dihydro-7-methoxy-3-(trifluoromethyl)-1H-benz[g]indazol-1-yl]benzenesulfonamide;

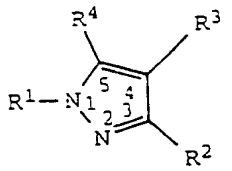
4-[4,5-dihydro-3-(trifluoromethyl)-1H-benz[g]indazol-1-yl]benzenesulfonamide;

4-[4,5-dihydro-7-methyl-3-(trifluoromethyl)-1H-benz[g]indazol-1-yl]benzenesulfonamide;

methyl[1-(4-aminosulfonylphenyl)-4,5-dihydro-7-methoxy-1H-benz[g]indazol-3-yl]carboxylate; and

4-[4,5-dihydro-3-trifluoromethyl-1H-thieno[3,2,g]indazol-1-yl]benzenesulfonamide.

10. A compound of Formula I



(I)

wherein R^1 is selected from phenyl, naphthyl, biphenyl, and five- or six-membered heteroaryl, wherein R^1 is substituted at a substitutable position with one or more radicals selected from halo, C_1-C_{10}-alkyl, C_1-C_6-alkoxy, hydroxyl and C_1-C_6-haloalkyl; wherein R^2 is selected from C_1-C_6-haloalkyl; wherein R^3 is hydrido; and wherein R^4 is aryl substituted at a substitutable position with sulfamyl;

wherein aryl wherever occuring means phenyl, naphthyl, tetrahydronaphthyl, indane, biphenyl;

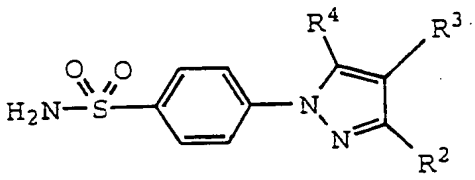
or a pharmaceutically-acceptable salt thereof.

11. Compound of Claim 10 selected from compounds, and their pharmaceutically acceptable salts, of the group consisting of

4-[1-(4-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-5-yl]benzenesulfonamide; and

4-[1-(4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-5-yl]benzenesulfonamide.

12. A compound of Formula II



(II)

wherein R^2 is selected from hydrido, C_1-C_{10}-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxycarbonyl, cyano, carboxyl,

C_1-C_6-cyanoalkyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, C_3-C_7-cycloalkylaminocarbonyl, arylaminocarbonyl, C_1-C_6-carboxyalkylaminocarbonyl, C_1-C_6-aralkoxycarbonyl-C_1-C_{10}-alkylaminocarbonyl, C_1-C_6-aminocarbonylalkyl, C_1-C_6-carboxyalkyl, C_1-C_6-alkoxycarbonylcyanoalkenyl and C_1-C_6-hydroxyalkyl;

wherein R^3 is selected from hydrido, C_1-C_{10}-alkyl, cyano, C_1-C_6-hydroxyalkyl, C_3-C_7-cycloalkyl, C_1-C_6-alkylsulfonyl and halo; and

wherein R^4 is selected from aryl-C_2-C_{10}-alkenyl, aryl, C_3-C_{10}-cycloalkyl, C_3-C_{10}-cycloalkenyl and heterocyclic; wherein R^4 is optionally substituted at a substitutable position with one or more radicals selected from halo, C_1-C_6-alkylthio, C_1-C_6-alkylsulfonyl, cyano, nitro, C_1-C_6-haloalkyl, C_1-C_{10}-alkyl, hydroxyl, C_2-C_6-alkenyl, C_1-C_6-hydroxyalkyl, carboxyl, C_3-C_7-cycloalkyl, C_1-C_6-alkylamino, C_1-C_{10}-dialkylamino, C_1-C_6-alkoxycarbonyl, aminocarbonyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, sulfamyl, five or six membered heterocyclic and amino; wherein aryl wherever occuring means phenyl, naphthyl, tetrahydronaphthyl, indane, biphenyl;

provided R^1 and R^3 are not both hydrido; further provided that R^2 is not carboxyl or methyl when R^3 is hydrido and when R^4 is phenyl; further provided that R^4 is not triazolyl when R^2 is methyl; further provided that R^4 is not aralkenyl when R^2 is carboxyl, aminocarbonyl or ethoxycarbonyl; further provided that R^4 is not phenyl when R^2 is methyl and R^3 is carboxyl; further provided that R^4 is not 4-chlorophenyl when R^2 is methyl and R^3 is bromo; further provided that R^4 is not unsubstituted thienyl when R^2 is trifluoromethyl;
or a pharmaceutically-acceptable salt thereof.

13. Compound of Claim 12 selected from compounds, and their pharmaceutically-acceptable salts, of the group consisting of

4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-phenyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-chlorophenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[3-(difluoromethyl)-5-(4-methylphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[3-(difluoromethyl)-5-phenyl-1H-pyrazol-1-yl]benzenesulfonamide;

4-[3-(difluoromethyl)-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[3-cyano-5-(4-fluorophenyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[3-(difluoromethyl)-5-(3-fluoro-4-methoxyphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-fluoro-4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

4-[4-chloro-5-phenyl-1H-pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-chlorophenyl)-3-(hydroxymethyl)-1H-pyrazol-1-yl]benzenesulfonamide; and

4-[5-(4-(N,N-dimethylamino)phenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide.

14. A pharmaceutical composition comprising a therapeutically-effective amount of a compound and a pharmaceutically-acceptable carrier or diluent, said compound selected from a family of compounds according to any of claims 1 to 13.

15. Use of a compound according to any of claims 1 to 13 for preparing a medicament for treating inflammation or an inflammation-associated disorder in a subject.

16. The method of Claim 15 for use in treatment of inflammation.

17. The method of Claim 15 for use in treatment of an inflammation-associated disorder.

18. The method of Claim 17 wherein the inflammation-associated disorder is arthritis.

19. The method of Claim 17 wherein the inflammation-associated disorder is pain.

20. The method of Claim 17 wherein the inflammation-associated disorder is fever.

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Applicant G. D. SEARLE & CO. et al	

The International Bureau transmits herewith the following documents and number thereof:

_____ copy of the international preliminary examination report and annexes (Article 36(3)(a))

This is a corrected version of the International Preliminary Examination Report which replaces and cancels the former version transmitted together with Form PCT/IB/310 dated : 18 December 1995 (18.12.95)

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